REMARKS

The Official Action of August 11, 2010 constitutes a non-final rejection of the claims. Favorable action on the merits is solicited in view of the foregoing amendments and the following remarks.

I. Claim Status and Amendments

Claims 106-111 were pending in this application when last examined and stand rejected. Applicants thank Examiner Swope for her time and consideration during the telephone interviews with the undersigned. See below for a summary thereof. As discussed in the interviews, Applicants again thank Examiner Swope for permitting Applicants to switch the examined invention from method claims to polypeptide claims.

By way of the present amendment, the claims have been amended to better clarify the nature of the invention. Support can be found throughout the general disclosure and claims. No new matter has been added.

Claim 109 has been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional on any cancelled subject matter.

Claims 106-108 and 110-111 are pending upon entry of this amendment, and these claims define patentable subject matter for the reasons discussed herein.

Applicants again wish to note that the polypeptide claims to SEQ ID NOS: 18 and 19 have been accepted in the corresponding EP application (EP 03 74 6399.9).

II. Priority

On page 2, the examiner indicates that the claims are only entitled to a priority date of April 15, 2003, which is the filing date of PCT/IL03/00317, because while the examiner can find support for SEQ ID NOS 18 and 19 in the PCT application, she cannot find support for such in the foreign priority documents (Israeli 14927 and 152183). In reply, Applicants wish to note that Israeli application 152183 does have SEQ ID NO. 18 and therefore fully supports this embodiment.

III. Provisional Double Patenting Rejection

On page 3 of the Office Action, the examiner provisionally rejects claims 106-108 under the judicially created doctrine of obviousness-type double patenting as being obvious over claim 8 of co-pending application No. 12/166,110. The examiner contends that claims 106-108 and claim 8 of the copending application are not patentably distinct because both are directed to peptides that bind to cgc. The examiner argues that claim 8 encompasses any peptide that inhibits binding between NIK and cgc, while claims 106-108 encompass fragments of SEQ ID NOS 18 and 19.

This is a provisional rejection, because the conflicting claims have not yet been patented. The rejection is respectfully traversed.

With respect to the double patenting rejection over the claims of co-pending application No. 12/166,110, Applicants respectfully disagree with the rejection. First of all, the rejection appears improper because dominance is not the same thing as obviousness. Just because claim 8 of copending application No. 12/166,110 may dominate claims 106-108 of the instant application, this does not mean that claims 106-108 would have been obvious from reading claim 8. For this reason, the rejection is improper and should be withdrawn.

In any event, Applicants note that claim 8 is a withdrawn claim. Applicants are considering deleting the withdrawn claims of the copending application, without prejudice, toward the filing of a divisional application. Such action would clearly obviate the rejection.

Lastly, Applicants again note that the rejection is a provisional rejection. In the event that the examiner disagrees with the above traversal and maintains the rejection, then Applicants hereby request that the provisional rejection be held in abeyance until the

conflicting claims are ready for patenting, as per US practice.

IV. Indefiniteness Rejections

Claims 106-111 have been rejected under 35 USC 112, second paragraph, for being indefinite for the reasons set forth on page 4 of the Office Action. The rejection is respectfully traversed. It is believed that the present amendment obviates the concerns raised in the Office Action for reasons which are self-evident.

The examiner contends that the claim language "640 to 720 of SEQ ID NO: 19" renders the claims indefinite because SEQ ID NO: 19 has only 324 resides. Applicants respectfully disagree with the rejection and fail to see how the noted language is confusing or indefinite. As discussed in the interview, the specification at page 20, lines 9-10 (paragraph [0071]) clearly discloses that a domain of NIK, responsible for cyc binding, comprises 81 amino acid residues from the C-terminus of NIK (from residue 624 to 947) (i.e., our SEQ ID NO: 19), named NIK640-720 (our SEQ ID NO: 18). This is also described in original claims 23 and 43. This indicates that SEQ ID NO: 18 (residues NIK640-720) is located within SEQ ID NO: 19 (residues 624 to 947). This supports element (c) of claims 106 and 107 that recites "a fragment of (a) or (b) that retains the ability to bind cyc

and includes residues 640 to 720 of SEQ ID NO: 19", as resides "640 to 720" fall within residues 624 to 947 of SEQ ID NO: 18. Further, as disclosed in the specification, "640 to 720 of SEQ ID NO: 19" is clearly encompassed by residues 624 to 947 (SEQ ID NO: 19). As such, the objected language is not inconsistent with the teachings in the disclosure.

In reply to the examiner's objection to the term "the carboxyl group", Applicants respectfully submit that the objected claim language is clear and definite for the following reasons. As set forth in MPEP § 2173.02 (Eighth Ed., Rev. 7 (July 2008)), definiteness of claim language is analyzed, not in a vacuum, but in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. Applicants respectfully submit that the specification, for instance, at paragraphs [0087 - 0088], clearly discloses and describes the noted claim language, and based on this disclosure, it is believed that the skilled artisan would understand the metes and bounds of this functional derivative language. The specification at paragraph [0089] defines "functional derivatives" as derivatives which can be prepared from the functional groups present <u>on the lateral chains of the amino acid moieties or on the terminal N- or C-groups</u> according to

known methods and are comprised in the invention when they are pharmaceutically acceptable i.e. when they do not destroy the protein activity or do not impart toxicity to the pharmaceutical compositions containing them. Such derivatives include for example esters or aliphatic amides of the carboxyl-groups and N-acyl derivatives of free amino groups or O-acyl derivatives of free hydroxyl-groups and are formed with acyl-groups as for example alcanoyl- or aroyl-groups. Based on this disclosure, the skilled artisan would clearly understand that the claim language "carboxyl groups" in elements (d) of claims 106, 107, and 108 refers to any carboxyl groups of said polypeptides. Further, such claim language is standard functional derivative language, and the making functional derivatives of active polypeptides are extremely well known in the art.

Based on the above, it is respectfully submitted that the claims are thus clear, definite and have full antecedent basis. The rejection is believed to be overcome, and withdrawal thereof is respectfully requested.

V. Enablement and Written Description Rejections

On page 5 of the Office Action, the examiner rejects claims 106-108 under 35 U.S.C. § 112, first paragraph, on the basis that the specification, while being enabling for polypeptides of SEQ ID NOS: 18 and 19, which

bind to a human bone marrow cγc protein, does not reasonably provide enablement for any fragment or variant thereof, of any polypeptide comprising or consisting of SEQ ID NO: 18 or 19, that bind to any cγc protein having any structure. The examiner contends that the claims are too broad and encompass a vast number of variants and fragments, and that it would take undue experimentation to produce and isolate peptides having the requisite activity from such variant polynucleotides. On page 6, the examiner contends that the disclosure is limited to the polypeptides of SEQ ID NO: 18 and 19, and on page 7, the examiner contends that the specification does not teach the structure of polypeptides having any cgc function, nor the regions of each protein's structure that may be modified without affecting the desired activity.

For essentially the same reasons, the examiner, on page 8, has rejected claims 106-108 under 35 U.S.C. § 112, first paragraph, on the basis that the specification lacks written description support for the broad genus of fragments and variants of any polypeptide comprising or consisting of SEQ ID NOL 18 or 19.

The rejections are respectfully traversed, as applied to the amended claims.

As discussed in the interviews, Applicants have amended the claims in a manner believed to overcome the rejections. With respect to the variants language, the claims have been amended to "a polypeptide having at least 95% identity with SEQ ID NO: 19" (or SEQ ID NO: 18) and to further specify that the polypeptide binds to the same cyc protein that SEQ ID NO: 19 (or SEQ ID NO: 18) binds to. With respect to the fragments embodiment, the claims have been similarly amended to specify that the fragment binds to the same cyc protein that the whole binds to. In this regard, Applicants note that they are not trying to claim a fragment of SEQ ID NO: 18 that binds to something that SEQ ID NO: 18 will not bind to. The same is true for SEQ ID NO: 19. Instead, Applicants intend to only claim fragments that bind to the same protein that SEQ ID NO: 18 and 19 bind to.

Further, it is believed that the specification provides clear written description and enabling support for the polypeptides of SEQ ID NOS: 18 and 19, as well as, fragments, variants having at least 95% identity and derivatives of SEQ ID NOS: 18 and 19. The specification shows the following:

> (i) the C-terminal fragment of NIK, residues 624-947 (SEQ ID NO: 19) binds cyc in a yeast two hybrid assay (Ex. 1) (page 43, line 17 to page 44, line 21);

> (ii) the C-terminal fragment of NIK, residues 624-947 (SEQ ID NO: 19) co-immunoprecipitates with cγc from transfected cells (Fig 2) (Ex. 2, page 45, lines 6-28);
>
> (iii) the C-terminal fragment of NIK, residues 624-947 (SEQ ID NO: 19) inhibits binding between full-length NIK and full-length cγc (e.g., Table 1, page 45), and
>
> (iv) the C-terminal fragment of NIK, residues 624-947 (SEQ ID NO: 19) inhibits NIK+cγc-induced and NIK-induced NFkB activation (Fig 5; and
>
> (v) SEQ ID NO: 18, residues 640-720, also binds to cγc (Table 4).

Applicants respectfully submit that all of this supports claims directed to the polypeptides of SEQ ID NOS: 18 and 19.

Further, as to SEQ ID NO: 18, residues 640-720, Applicants point to Table 4 on page 57 as evidence that this sequence binds to cγc (Table 4). This Table shows that the cγc binding region in NIK resides in 196 amino acids at the C-terminus of SEQ ID NO: 19, which in turn corresponds to residues 640-720 (SEQ ID NO: 18). Also, the specification discloses that the C-terminal fragment of NIK1 (consisting of SEQ ID NO: 18) binds a cγc in the yeast two-hybrid system and that a NIK1 and a cγc are co-immunoprecipitated from cells over-expressing these proteins (Examples 1-2). See also Example 7 (on page 57), which shows the binding of a

NIK C-terminus peptide (NIK624-947) (SEQ ID NO: 19) is '++++' with full-length common gamma chain. The specification, at page 20, lines 9-10, also clearly discloses that the NIK624-947 (SEQ ID NO: 19) comprises the claimed peptide, SEQ ID NO: 18 (NIK640-720), and that the latter peptide contains the important cγc binding domain of NIK. Since the claimed peptide of SEQ ID NO: 18 (NIK640-720) contains the important cγc binding domain of NIK624-947 (SEQ ID NO: 19), then it stands to reason that it too binds to cγc in the same manner as NIK624-947.

It is respectfully submitted that the skilled artisan, upon reading the disclosure and in view of the knowledge in the art, would be able to make the limited number of fragments, derivatives and polypeptides having at least 95% and then test and determine which ones retain the requisite binding activity, as recited in the claims, using routine procedures, and without undue experimentation.

For these reasons, it is respectfully submitted that the specification clearly provides written description and enabling support for the polypeptides of the polypeptides of SEQ ID NOS: 18 and 19, as well as the fragments, derivatives and polypeptides having at least 95% thereof. Withdrawal of the rejections is requested.

VI. Prior Art Rejection

On page 9, claims 106, 107, and 109 are rejected under 35 U.S.C. § 102(b) as being anticipated by Wallach et al., 1997 (IDS; WO9737016). The examiner contends that Wallach et al., 1997 teaches human NIK, as well as the fragment of human NIK set forth by SEQ ID NO: 19 (example 5). The rejection is respectfully traversed as applied to the amended claims.

As to the art rejection, it appears that prior art example 5 does indeed teach the entire SEQ ID NO. 19, *per se*, although it does not disclose Applicants' use. Nor does it disclose the fragments, variants, thereof. For the sole purpose of expediting prosecution and not to acquiesce to the rejection, the claims 106 and 107 have been amended to delete sub-paragraph (a), i.e., the polypeptide of SEQ ID NO: 19. In other words, the claims no longer claim just SEQ ID NO: 19, but instead only the variants and fragments thereof. In doing so, the present amendment obviates the rejection, because Wallach et al., 1997 (IDS; WO9737016) does not disclose the fragments, variants, etc. as claimed.

VII. Conclusion

Applicant believes that all issues raised in the Official Action have been fully addressed in a manner that

should lead to patentability of the present application. Favorable consideration and allowance are requested.

Applicants again thank Examiner Swope for her time and effort in the interviews with the undersigned. If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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